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Pesticide Fact Sheet Number 48.1-Picloram

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16. Abstract (Limit: 200 words)

This document contains up-to-date chemical information, including a summary of the Agency's regulatory position and rationale, on a specific pesticide or group of pesticides. A Fact Sheet is issued after one of the the following actions has occurred.

1. Issuance or reissuance of a registration standard,
2. Issuance of each special review document,
3. Registration of a significantly changed use pattern,
4. Registration of a new chemical, or
5. An immediate need for information to resolve controversial issues relating to a specific chemical or use pattern.

17. Document Analysis a. Descriptors

Pesticides, regulations, Chemical Information Fact Sheet, Use Patterns, science findings.

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

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EPA

Pesticide Fact Sheet

Name of Chemical: Picloram
Reason for Issuance: Registration Standard
Date Issued: October 24, 1988
Fact Sheet Number: 48.1

1. Description of Chemical

Chemical Name: 4-amino-3,5,6-trichloropicolinic acid
Common Name: Picloram
OPP Chemical Code: 005101
Chemical Abstracts Service (CAS) Number: 1918-02-1
Year of Initial Registration: 1964
Pesticide Type: Herbicide
Chemical Family: Picolinic acid
U.S. Producer: Dow Chemical, U.S.A.

Chemical Name: Potassium salt of 4-amino-3,5,6-trichloropicolinic acid
Common Name: Picloram, Potassium (K) salt
OPP Chemical Code: 005104
CAS No.: 2545-60-0

Chemical Name: Isooctyl ester of 4-amino-3,5,6-trichloropicolinic acid
Common Name: Picloram, Isooctyl ester (IOE) of picloram
OPP Chemical Code: 005103

Chemical Name: Triisopropanolamine salt of 4-amino-3,5,6-trichloropicolinic acid
Common Name: Picloram, TIPA salt
OPP Chemical Code: 005102

Chemical Name: Triethylamine salt of 4-amino-3,5,6-trichloropicolinic acid
Common Name: Picloram, TEA salt
OPP Chemical Code: 005105

Chemical Name: Isopropanolamine salt of 4-amino-3,5,6-trichloropicolinic acid
Common Name: Picloram, IPA salt

2. Use Patterns and Formulations

Application Sites:

Picloram, potassium salt: Terrestrial food crop use on small grains, flax, pastures and rangeland grasses; Terrestrial noncrop use on noncrop agricultural areas and rights-of-way; Forestry use on forest lands site preparation.

Picloram, isooctyl ester: Terrestrial noncrop use on industrial sites and rights-of-way; Forestry use on forest trees site preparation.

Picloram triisopropanolamine salt: Terrestrial food crop use on small grains and pastures and rangeland; Terrestrial nonfood crop use on uncultivated agricultural areas, rights-of-way, and industrial sites; Aquatic noncrop use on drainage ditch banks; Forestry use on forest trees.

Picloram, triethylamine salt: Terrestrial food crop use on pastures and rangelands.

Types and Methods of Application: By ground: broadcast or spot treatment as foliar or soil spray; as a basal spot treatment, broadcast as pelletized spray; as tree injection, as frill treatment; as a stump treatment, as basal bark treatment, as a wick application, and as a low-volume dormant stem spray. By air: broadcast and low-volume dormant spray.

Pests Controlled: Broadleaf weeds and woody plants.

Application Rates: (Section 3 registrations)

Picloram, TIPA salt: 0.27 to 3.00 pounds acid equivalent (lb ae) per acre (A)
Picloram, IOE: 0.5 to 3.0 lb ae/A(mixtures or MAF)
Picloram, K salt: 1.0 to 8.5 lb ae/A
Picloram, TEA salt: 0.25 to 1.0 lb ae/A(SLNS)

Types of Formulations: [represented Sec 3 registrations of the potassium salt(K)]: Formulation Intermediate: 30% ae or 34.7% acvtive ingredient (ai), Pelleted: 2% ae or 2.3 ai, 5 ae or 5.8% ai, 10% ae or 11.6 ai; Soluble Concentrate, Liquid: 2 lb ae or 24% ai, 24.4% ai or 29.9% ai

Usual Carrier: Water

3. Science Findings

Summary Science Statement: Technical picloram is in Toxicity Category I with respect to acute inhalation and Categories III and

IV with respect to other acute toxicities. Picloram has been classified as Group D Oncogen (not classifiable to human carcinogenicity). Repeat oncogenicity, teratology, and reproduction studies are being required. Picloram does not appear to be mutagenic based on available data.

Picloram is stable to hydrolysis, does not photodegrade under light, and is relatively stable in anaerobic loam soils and under anaerobic aquatic conditions and does not accumulate in fish. Picloram is intermediately to very mobile in soils ranging in texture from clay to loam. Picloram has been identified as a chemical with a potential to contaminate groundwater.

The Agency is requiring that residue data depicting residues of HCB in plant and animal commodities be submitted.

Picloram is practically nontoxic to avian species, slightly to moderately toxic to freshwater fish, and slightly toxic to freshwater invertebrates.

Chemical Characteristics:

Technical Picloram (Acid):
- Color: White
- Physical State: Powder
- Odor: Chlorine like
- Melting Point: 215 °C (decomposes)
- Bulk Density: 19.7 lb/cu ft
- Solubility at 25 °C:
  - 0.043 g/100 mL - Water
  - 0.55 g/100 mL - Isopropanol
  - 1.05 g/100 mL - Ethanol
  - 1.98 g/100 mL - Acetone
  - 0.12 g/100 mL - Diethyl ether
  - 0.16 g/100 mL - Acetonitrile
  - 1.85 g/100 mL - Methanol
  - 0.06 g/100 mL - Methylene dichloride
  - 0.02 g/100 mL - Benzene
  - 0.001 g/100 mL - Kerosene
- Vapor Pressure: 6.16×10^{-7} millimeters (mm) Hg at 35 °C
  1.07×10^{-6} mm Hg at 45 °C
- Storage Stability: Stable under normal conditions.

Picloram, Potassium (K) Salt (34.7% ai)
- Color: Dark brown
- Physical State: Liquid
- Odor: Alcoholic
- Bulk Density: 1.320 at 20 °C

Toxicology Characteristics:

Existing data are all based on picloram (technical) or K salt. Further data are requested for the IOE, TIPA salt, TEA salt, and IPA salt.

Acute Toxicology - Technical (Acid):

- o Acute Oral Toxicity (Rats): Greater than (>) 5000 mg/kg body weight for males - Toxicity Category IV; = 4012 mg/kg for females - Toxicity Category III
- o Acute Dermal Toxicity (Rabbits): > 2000 mg/kg for males and females, Toxicity Category III
- o Acute Inhalation (Rat): > 0.035 mg/L for males and females, Toxicity Category I
- o Primary Eye Irritation (Rabbit): Moderate eye irritation, Toxicity Category III
- o Primary Dermal Irritation (Rabbit): Not an irritant, Toxicity Category IV
- o Dermal Sensitization (Guinea Pig): Not a skin sensitizer

Acute Toxicology (K Salt):

- o Acute Oral Toxicity (Rat): > 5000 mg/kg for males, Toxicity Category IV; = 3536 mg/kg for females, Toxicity Category II
- o Acute Dermal Toxicity (Rabbit): > 2000 mg/kg for males and females, Toxicity Category III
- o Acute Inhalation Toxicity (Rat): > 1.5 mg/L for males and females, Toxicity Category II
- o Primary Eye Irritation (Rabbit): Moderate eye irritation, Toxicity Category III
- o Primary Dermal Irritation (Rabbit): Not a skin irritant, Toxicity Category IV
- o Dermal Sensitization (Guinea Pig): Skin Sensitizer*

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*Requires statement for skin sensitization: "May Cause Allergic Skin Reaction."

Acute Toxicology (IOE):

- o Acute Oral Toxicity (Rat): > 3500 mg/kg for males and females, Toxicity Category III
- o Acute Dermal Toxicity (Rabbit): > 2000 mg/kg for males and females, Toxicity Category III
- o Acute Inhalation Toxicity (Rats): > 0.35 mg/L for males and females, Toxicity Category II
- o Primary Eye Irritation (Rabbits): Moderate eye irritation, Toxicity Category III
- o Primary Dermal Irritation (Rabbit): Mild skin irritation, Toxicity Category III

Subchronic Toxicology Studies:

An acceptable 13-week subchronic feeding study in rats is available for picloram. The no-observed-effect level (NOEL) for this study was 50 mg/kg. A dose dependent increase in absolute and relative liver weights was seen at 150 mg/kg.

An acceptable 6-month feeding study with dogs is available for picloram. The NOEL for this study was 7 mg/kg. A decrease in food consumption and increase in liver weights was noted at the highest dose.

No subchronic feeding studies are available for the TIPA, TEA, IPA, or IOE forms of picloram. Subchronic feeding studies are required in a rodent and a nonrodent for each form of picloram.

A 21-day subchronic dermal study is not available for picloram. This study is required for all forms of picloram.

Chronic Feeding Studies:

An acceptable 2-year chronic feeding study with rats is available for picloram. An increase in size and altered tinctorial properties of centrilobular hepatocytes occurred in males and females at the high (200 mg/kg/day) and mid (60 mg/kg/day) dose resulting in a NOEL of 20 mg/kg/day for this study.

A chronic feeding study in nonrodents is not available for picloram and is required.

Oncogenicity Studies:

The available oncogenic data for picloram include mouse and rat studies performed by the National Toxicology Program (NTP) and a rat study performed by Dow Chemical U.S.A.

An oncogenic effect (neoplastic nodules) was seen in female rats at the highest dose in the NTP study. This study was unacceptable based on experimental design (too short exposure limit, insufficient information to determine if a maximum tolerated dose [MTD] was attained).

No oncogenic effects were noted in either the mouse study done by NTP or the rat study done by Dow. These studies were not acceptable because the available information was insufficient for determining if an MTD had been reached.

The test material in all of these studies contained the contaminant hexachlorobenzene (HCB), which is classified by the Agency as a Group B2 oncogen (probable human carcinogen). Picloram was classified as a Group D oncogen (not classifiable as to human carcinogenicity). The Agency is requiring that both the mouse and rat oncogenicity studies be repeated.

Teratogenicity and Reproduction:

A teratogenicity study in rabbits is available for picloram. A small number of fetuses showed abnormalities such as missing ribs, omphalocele, and hypoplastic tail. Historical control data are required to evaluate the observed abnormalities.

A teratology study in rats is available for picloram. No teratogenic effects were noted. Some fetotoxicity was present at the lowest dose. Because a NOEL cannot be set for the study a repeat teratology study in rats is required.

A multigeneration reproduction study in rat is available for picloram. No reproductive effects were observed however, too few test animals were used and no toxicity was observed at the highest dose. Therefore, a 2-generation reproduction study is required for picloram.

No teratology or reproduction studies are available for the ester and amine forms of picloram. Teratology studies in rats and rabbits are required for all ester and amine forms of picloram. Reproduction studies are not required at this time.

Mutagenicity:

Picloram did not show evidence of chromosomal changes in a cytogenetic bone marrow study exposing rats up to 2000 mg/kg of picloram.

No other acceptable mutagenicity studies are available for picloram, its salt, ester, or amine forms. Additional mutagenicity data are required for picloram, its esters, and its amines.

Metabolism:

Available rat metabolism data are not adequate to fulfill Guideline requirements; therefore, additional studies are required.

Manufacturing Contaminants:

Technical picloram is contaminated with HCB, classified as a probable human carcinogen (Group B2). Dietary and nondietary risk assessments were performed by the Agency. The Agency considered the dietary and nondietary risk from HCB to be acceptable at this time.

Nitrosoamines are a potential contaminant of tertiary amines (TEA) and alkanolamines (TIPA) forms of picloram. Testing is required to show that the level of 1 ppm nitrosoamine contamination is not exceeded.

Physiological and Biochemical Characteristics:

Foliar Absorption and Translocation: Picloram translocates from both the roots and leaves of plants and accumulates in the new growth. Picloram is both foliar-absorbed and root-absorbed.

Mechanism of Pesticidal Action: Alters nucleic acid and protein synthesis.

Metabolism and Persistence in Plants: Available plant metabolism data indicate that picloram degrades to CO_2, oxalic acid, and the metabolites 4-amino-2,3,5-trichloropyridine and 4-amino-3,5-dichloro-6-hydroxypicolinic acid.

Metabolism and Persistence in Animals: Available metabolism data indicate that animals excrete 82 to 98 percent of the [^{14}C]picloram used in dosing the animals as picloram.

Environmental Characteristics:

Absorption and Leaching in Basic Soil Types: Available data indicate that picloram was intermediately mobile to very mobile in soils ranging in texture from clay to loam. Adsorption of picloram pH. Addition of inorganic salts to the soil did not affect adsorption of picloram.

Microbial Breakdown: Picloram degraded with half-lives of 100 to 200 days in loam soil, 200 to 300 days in silt loam soil, and greater than 300 days in loamy sand, commerce loam, clay, and sandy loam soils under aerobic conditions. Picloram was relatively stable in anaerobic loam soil under anaerobic aquatic soil conditions.

Loss from Photodecomposition: Does not degrade.

Bioaccumulation in Fish: Does not accumulate in fish.

Potential to Contaminate Groundwater: Picloram has been previously identified as a pesticide with a propensity to leach into groundwater. Picloram has been reported as detected in seven States. Picloram is persistent and mobile and has a high potential to reach groundwater.

Exposure to Humans: Based on available acute toxicology data the major routes of exposure appear to be through inhalation and dermal sensitization. Although technical picloram (free acid) is in Toxicity Category I based on inhalation, there is little chance of exposure to mixer/loaders or applicators because there are currently no products registered containing the free acid form of picloram.

Risk to Humans: The major risk to humans appears to be from the contaminant HCB. Both dietary and nondietary risk assessments were performed. The dietary exposure to HCB occurs from the use of pesticides containing picloram on small grains and secondary residues on animal commodities. The oncogenic risk for the U.S. population based on dietary exposure was calculated to be $6. \times 10^{-7}$.

Potential nondietary exposure to HCB is to workers, mixer/loaders and applicators from use of picloram on wheat, forests, rights-of-way, and pasture/rangeland. The estimated nondietary risk to mixer/loaders and applicators ranged from 5.0×10^{-5} to 10^{-8}.

Reentry: Reentry intervals are not required because cultural practices for existing uses indicate little likelihood that field workers would be exposed to acutely toxic levels of picloram from agricultural applications.

Ecological Characteristics:

Avian Acute Oral Toxicity (Technical): Bobwhite quail > 2250 mg/kg/day; K Salt: Bobwhite quail > 2510 mg/kg/day

Avian Subacute Dietary Toxicity (Technical): Bobwhite quail > 5000 ppm, mallard duck > 5000 ppm; K Salt, bobwhite quail > 5620 ppm; IOE, bobwhite quail > 5620 ppm

Acute Toxicity to Freshwater Fish (Technical): Rainbow trout = 4.3 to 19.3 ppm, bluegill sunfish = 14.5 to 23.0 ppm; K Salt, rainbow trout = 13 ppm, catfish = 14 ppm, bluegill sunfish = 24 ppm; IOE, rainbow trout = 4.0 ppm, catfish = 1.4 ppm, bluegill sunfish = 6.3 ppm

Fish Embryolarvae Study: Rainbow trout with a maximum acceptable threshold concentration (MATC) = 0.55 < MATC < 0.88 mg/L

Acute Toxicity to Freshwater Invertebrates Studies: (Daphnids, Gammarus, Pteronarcella, and Pteronarcys) = 10 to 68.3 ppm

Chronic Aquatic Invertebrate Study (Daphnids): 11.8 < MATC < 18.1 mg/L

Acute Toxicity to Honey Bees (Technical): = 14.5 micrograms per bee

Technical picloram appears to be moderately to slightly toxic to freshwater fish, slightly toxic to aquatic invertebrates, and practically nontoxic to birds. Chronic fish testing showed that picloram caused a reduction in rainbow trout larval survival at 2.02 mg/L and a reduction in growth at 0.88 mg/L. Picloram affected the growth and survival in cutthroat trout at 0.29 mg/L.

The isooctyl ester form of picloram is moderately toxic to fish, and practically nontoxic to birds.

The potassium salt of picloram appears to be slightly toxic to freshwater fish and practically nontoxic to birds.

Phytotoxicity and Endangered Species

Picloram has been shown to be a highly phyotoxic herbicide.

Because of picloram's demonstrated toxicity to nontarget plant species and its intended use pattern, picloram has been identified as being likely to jeopardize endangered plant species when used on pastures/rangeland and forests. A program is being developed by the Agency to reduce or eliminate exposure to these species to a point where use does not jeopardize these species.

Tolerance Assessment:

Tolerances are established under 40 CFR 180.292 for residues of the picloram. Food and Feed additive tolerance are established under 40CFR 185.4580 and 40 CFR 186.4580. These replace old Section 21 CFR 183.350 and 21 CFR 561.305.

The Agency has established a R.F.D or a provisional acceptable daily intake at 0.07 mg/kg/day based on a 6-month dog feeding study (NOEL of 7.0 mg/kg/day) using a safety factor of 100. The theoretical maximum residue contribution (TMRC) is calculated to be 0.001847 mg/kg/day, which utilizes 2.6 percent of the PADI.

The tolerance assessment indicated that additional residue data are needed for wheat grain, wheat forage, wheat straw, pasture, rangeland grasses, and flax. Data are required depicting residues of HCB in or on wheat grain, wheat straw, pasture and rangeland grasses, flax seed, and flax straw. Additional plant and animal metabolism data are needed.

Reported Pesticide Incidents

Most of the reported pesticide incidents involve crop damage and damage to other nontarget plants resulting from drift and from soil contaminated with picloram.

4. Summary of Regulatory Position and Rationale

A review of available data indicates that none of the risk criteria listed in 40 CFR 154.7 have been exceeded. Therefore, no referral to Special Review is being made at this time.

The Agency will continue to require that EPs containing picloram retain the "Restricted Use" classification and the groundwater advisory against the use of picloram on well-drained soils.

The Agency is requiring that the rat and mouse oncogenicity studies be repeated using Osborne-Mendel rats and $B_6C_3F_1$ mice of both

sexes using a commercially available technical grade picloram uncontaminated with potentially tumorigenic levels of HCB.

The Agency has determined that basic toxicology studies are needed for the organic esters and amines of picloram in addition to the complete toxicological testing of the acid and/or K salt.

The Agency will continue to require manufacturers to limit the level of HCB in the technical to a maximum of 200 ppm.

The Agency is requiring nitrosamine testing for the tertiary amine and alkanoloamine forms of picloram. The level of nitrosoamines permitted in these forms is a maximum of 1 ppm.

The Agency is requiring that a prospective groundwater monitoring study be submitted for picloram.

The Agency is requiring that Tier II phytotoxicity testing be performed with the technical picloram, its salts, ester, and amine forms.

The Agency is requiring that droplet size spectrum and drift field evaluation data be submitted for picloram.

The Agency is requiring that additional residue data be submitted for wheat grain, wheat forage, wheat straw, pasture and rangeland grasses, and flax. The data must include residues of HCB and the results of analysis for HCB levels.

The Agency is requiring that additional plant metabolism data be submitted providing complete identification and quantitation of all terminal residues.

The U. S. Fish and Wildlife Service has determined that picloram is likely to jeopardize endangered plant species when used on rangeland/pastureland and forests. The Agency is developing a program to reduce or eliminate exposure of this chemical to these species. After the program is developed, notification of any additional labeling requirements will be made.

The Agency is requiring that the labels of products containing picloram determined to be skin sensitizers include the statement "May cause allergic skin reaction after multiple exposure" on the labels

The Agency will not approve any significant new food uses for picloram while major data gaps exist. When additional data are evaluated the Agency will determine whether significant new uses may be established.

B136/10

5. Summary of Data Gaps

Requirements	Due Dates
Product Chemistry	6 to 15 months
Residue Data	6 to 24 months
Toxicology Data	9 to 40 months
Environmental Fate	9 to 39 months
Groundwater Monitoring	9 months
Plant Protection	9 months

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